510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K213858

B Applicant

DiaSorin Inc.

C Proprietary and Established Names

LIAISON Calprotectin

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
NXO	Class II	21 CFR 866.5180 - Fecal Calprotectin Immunological Test System	IM - Immunology

II Submission/Device Overview:

A Purpose for Submission:

Modification of a cleared device – Addition of the LIAISON Q.S.E.T. Device Plus as stool sample collection and extraction accessory to the cleared LIAISON Calprotectin

B Measurand:

Calprotectin

C Type of Test:

Quantitative, automated immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The DiaSorin LIAISON Calprotectin assay is an in vitro diagnostic chemiluminescent immunoassay (CLIA) intended for the quantitative measurement, in human stool, of fecal calprotectin, a neutrophilic protein that is a marker of mucosal inflammation. The LIAISON Calprotectin assay can be used as an aid in the diagnosis of inflammatory bowel diseases (IBD), specifically Crohn's disease and ulcerative colitis, and as an aid in differentiation of IBD from irritable bowel syndrome (IBS). Test results are to be used in conjunction with information obtained from the patients' clinical evaluation and other diagnostic procedures. The test has to be performed on the LIAISON Analyzer Family.

The DiaSorin LIAISON Q.S.E.T. Device Plus (Quantitative Stool Extraction and Test) is intended for use in the preparation of human stool specimens for testing in the LIAISON Calprotectin assay.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

LIAISON XL Analyzer (K181464)
LIAISON XS Analyzer (K193532)

IV Device/System Characteristics:

A Device Description:

Refer to K182698 for the DiaSorin LIAISON Calprotectin reagent system. Reagent formulations for the LIAISON Calprotectin assay are unchanged.

LIAISON Q.S.E.T Device Plus (*optional*): The device consists of a polypropylene tube containing 6.0 mL of LIAISON Q.S.E.T. extraction buffer, and a stick shaped with grooves for collecting the sample. The blue upper cap end of the device contains the sample wand, and can be separated from the black inner cap which eliminates excess material from the collection tube containing extraction buffer. Separate instructions are provided for pipetting 12 µL of liquid sample (e.g. Bristol Stool Form Scale [BSFS] type 7) directly into the collection tube of the LIAISON Q.S.E.T. Plus from liquid stool samples. Design, manufacturing, and materials are similar to the Q.S.E.T. extraction device cleared in K182698.

B Principle of Operation:

Refer to K182698 for Test Principle of the LIAISON Calprotectin assay.

The optional Q.S.E.T. Plus device collects the amount of stool required to perform the LIAISON Calprotectin assay directly from a primary specimen container instead of manually weighing the sample, or using the alternate, cleared Q.S.E.T. device. Following extraction with the Q.S.E.T. Plus device, the sample can be used the LIAISON Calprotectin assay procedure, per K182698.

Pre-analytical processing of fecal samples is accomplished by either manual weight normalization, followed by homogenization in Q.S.E.T. buffer (per K182698); or by using the optional Q.S.E.T (per K182698) or Q.S.E.T. Plus devices for sample collection and homogenization. The Q.S.E.T Device Plus may be loaded directly onto LIAISON XL or LIAISON XS analyzer sample racks.

Following measurement, the assay reports calprotectin concentrations in units of microgram-per-gram of starting fecal sample material (µg/g). Interpretation of fecal calprotectin concentration [fCal] is as follows:

[fCal] (µg/g)	Interpretation
< 50 µg/g	Negative
50 – 120 µg/g	Borderline
>120 µg/g	Positive

V Substantial Equivalence Information:

A Predicate Device Name(s):

LIAISON Calprotectin
LIAISON Q.S.E.T. Device

B Predicate 510(k) Number(s):

K182698

C Comparison with Predicate(s):

Device & Predicate Device(s):	**K213858**	**K182698**
Device Trade Name(s)	LIAISON Calprotectin LIAISON Q.S.E.T. Device Plus	LIAISON Calprotectin LIAISON Q.S.E.T. Device
General Device Characteristic Similarities		
Intended Use/ Indications For Use	The DiaSorin LIAISON Calprotectin assay is an *in vitro* diagnostic chemiluminescent immunoassay (CLIA) intended for the quantitative measurement, in human stool, of fecal calprotectin, a neutrophilic protein that is a marker of mucosal inflammation.	The DiaSorin LIAISON Calprotectin assay is an *in vitro* diagnostic chemiluminescent immunoassay (CLIA) intended for the quantitative measurement, in human stool, of fecal calprotectin, a neutrophilic protein that is a marker of mucosal inflammation.

	The LIAISON Calprotectin assay can be used as an aid in the diagnosis of inflammatory bowel diseases (IBD), specifically Crohn's disease and ulcerative colitis, and as an aid in differentiation of IBD from irritable bowel syndrome (IBS). Test results are to be used in conjunction with information obtained from the patients' clinical evaluation and other diagnostic procedures. The test has to be performed on the LIAISON Analyzer Family. The DiaSorin LIAISON Q.S.E.T. Device Plus (Quantitative Stool Extraction and Test) is intended for use in the preparation of human stool specimens for testing in the LIAISON Calprotectin assay.	The LIAISON Calprotectin assay can be used as an aid in the diagnosis of inflammatory bowel diseases (IBD), specifically Crohn's disease and ulcerative colitis, and as an aid in differentiation of IBD from irritable bowel syndrome (IBS). Test results are to be used in conjunction with information obtained from the patients' clinical evaluation and other diagnostic procedures. The test has to be performed on the LIAISON XL Analyzer. The DiaSorin LIAISON Q.S.E.T. Device (Quantitative Stool Extraction and Test) is intended for use in the preparation of human stool specimens for testing in the LIAISON Calprotectin assay.
Specimen Sampling	Unitized specimen probe and sample extraction device	Same
Sample normalization	Volumetric	Same
Assay processing	Automated	Same
Instrumentation	LIAISON XL and XS Analyzers	Same
Assay Methodology	Solid-phase (heterogeneous) immunoassay	Same
Solid-phase	Paramagnetic microparticles	Same
Capture antibodies	Mouse monoclonal anti-human calprotectin	Same
Detection antibodies	Mouse monoclonal anti-human calprotectin	Same
Detection chemistry	Isoluminol chemiluminescence	Same
Assay Output	Quantitative	Same
Measurand	Human calprotectin	Same
Antigen	Recombinant human calprotectin	Same
Interpretation	Normal: <50 µg/g Borderline: 50 – 120 µg/g Elevated: >120 µg/g	Same
Primary measurement units	Relative Light Units (RLU)	Same
Analytical Measuring Range	5.0 – 800.0 µg/g	Same

Extended Analytical Measuring Range	Automated 1:10 dilution: 800.0 – 8000 µg/g	Same
General Device Characteristic Differences		
Extraction buffer	6.0 mL pre-loaded extraction buffer	6.0 mL, separate extraction buffer to be added by user
Stool sample specifications	Bristol Stool Form Scale (BSFS) 2−7	BSFS 2−6
Shelf-Life	12 months @ 2−8°C 12 months @ 20−24°C	18 months @ 2−8°C
Sample Stability, without centrifugation	16 weeks @ -20°C 72 hours @ 2−8°C 6 hours @ 20−24°C	6 hours @ 2−8°C 4 hours @ 20−24°C
Sample Stability, with centrifugation	7 days @ -20°C 1× freeze-thaw cycle	8 days @ 2−8°C

VI Standards/Guidance Documents Referenced:

CLSI EP05-A3, "Evaluation of Precision of Quantitative Measurement Procedures"

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

Analytical studies for the Q.S.E.T. Device Plus were performed with the LIAISON Calprotectin assay using the LIAISON XL analyzer.

1. Precision/Reproducibility:

Q.S.E.T. Device Plus Sample Weight Validation

The manufacturer performed a study evaluating the precision of the amount of the sample collected by the Q.S.E.T. Device Plus sample collection device. Five stool specimens ranging from Types 2–7 on the Bristol Stool Form Scale (BSFS) were sampled by three operators with five replicates per sample per operator, using three lots of the Q.S.E.T. Device Plus sample collection device. Samples on the Q.S.E.T. Device Plus sample collection device were weighed against the empty weight of the Q.S.E.T. Device Plus device. Results of the study are summarized below:

Precision of Q.S.E.T. Device Plus Sample Weight										
Sample	BSFS	Mean Weight (mg)	Repeatability		Between-Operator		Between-Lot		Within-Lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	2	10.23	1.05	10.29	0.00	0.00	0.00	0.00	1.05	10.29
2	4	11.02	0.87	7.91	0.00	0.00	0.00	0.00	0.87	7.91
3	5	11.79	0.73	6.21	0.00	0.00	0.00	0.00	0.73	6.21
4	6	12.00	0.67	5.56	0.00	0.00	0.25	2.04	0.71	5.93
5	7	11.39	0.84	7.37	0.36	3.14	0.00	0.00	0.91	8.01

The overall precision of sample collection weight was assessed across all five samples, replicates, operators, and lots. The sample weight collected by the Q.S.E.T. Plus is described in the table below:

Sample collection performance of Q.S.E.T. Device Plus	
Mean Sample Weight	11.3 mg
Median Sample Weight	11.4 mg
Range	8.5–13.5 mg
95% CI	11.2–11.4 mg
Standard Deviation	1.06 mg
% Coefficient of Variation	9.38%

Assay Reproducibility

To evaluate the reproducibility of the assay using the Q.S.E.T. Device Plus sample collection device, each of five stool samples representing concentrations spanning the analytical measuring interval (AMI) were extracted daily using the Q.S.E.T. Plus by three operators independently for five days. Extracted samples were tested in one run per day, six replicates per run using one reagent lot by three operators for five days to generate a total of 90 datapoints per sample. The results of this study are summarized below:

LIAISON fecal calprotectin reproducibility, using the Q.S.E.T. Device Plus												
Sample	N	Mean (µg/g)	Repeatability		Between-Day		Within-Operator		Between-Operator		Total	
			SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
1	90	17.2	0.42	2.5	1.39	8.1	1.45	8.4	1.26	7.3	1.81	10.5
2	90	37.9	0.88	2.3	5.63	14.9	5.69	15.0	4.29	11.3	6.67	17.6
3	90	120	2.43	2.0	12.1	10.1	12.3	10.3	6.29	5.2	12.7	10.6
4	90	264	7.27	2.8	29.3	11.1	30.3	11.4	24.5	9.3	36.5	13.8
5	90	1018	36.3	3.6	119	11.7	124	12.1	69.4	6.8	131	12.9

2. Linearity:

Linearity for the LIAISON Calprotectin assay was evaluated in K182698.

3. Analytical Specificity/Interference:

Interference for the LIAISON Calprotectin assay was evaluated in K182698.

4. Assay Reportable Range:

The assay reportable range for the LIAISON Calprotectin assay was evaluated in K182698.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Traceability:

Refer to K182698

Reagent Stability:

Refer to K182698 for the reagent kit stability of the LIAISON Calprotectin assay.

Q.S.E.T. Device Plus Stability:

Evaluations of the stability of the Q.S.E.T. Device Plus component, containing buffer were performed on three lots × five timepoints × two temperature conditions, in real-time. The analysis methods, set at an acceptance threshold of ±10% difference from baseline (t_0) were consistent with the recommendations in CLSI EP25-A. Results are summarized below:

Component	Storage Conditions	Shelf-Life
Q.S.E.T. Device Plus	2–8°C	12 months
Q.S.E.T. Device Plus	20–24°C	12 months

Sample Stability:

Critical storage parameters for stool samples were determined for stability, using six samples collected with the Q.S.E.T. Device Plus stored under the conditions in the table below for a minimum of five timepoints, and tested with the LIAISON Calprotectin assay. Acceptable stability duration claims are based on one timepoint prior to the last timepoint with the assay result < ±10% difference from baseline (t_0). Conclusions from these sample stability studies are summarized below:

Sample Format	Conditions	Stability
Unextracted sample	-20°C	16 weeks
Unextracted sample	2–8°C	72 hours
Unextracted sample	20–24°C	6 hours
Q.S.E.T. Device Plus, containing extracted sample	-20°C	7 days
Q.S.E.T. Device Plus, containing extracted sample	freeze-thaw	1 freeze-thaw cycle

6. Detection Limit:

The detection capabilities (i.e. Limit of Blank (LoB), Limit of Detection (LoD), Limit of Quantitation (LoQ)) for the LIAISON Calprotectin assay were evaluated in K182698.

7. Assay Cut-Off:

The assay cut-off for the LIAISON Calprotectin assay was evaluated in K182698.

B Comparison Studies:

1. Method Comparison with Predicate Device:

One-hundred eighty-three (183) human stool samples selected to represent the span of the AMI were extracted with one lot of the Q.S.E.T. Device Plus, as well as one lot of the Q.S.E.T. predicate device. Paired samples from both processing methods were tested in singlicate by the LIAISON Calprotectin assay. Samples outside the valid AMI were excluded for a final *n* = 159. Passing-Bablok regression parameters were calculated and summarized in the following table:

	Q.S.E.T. Device Plus vs. Q.S.E.T. Device
n	159
Range	5−741 µg/g
Slope (95% CI)	0.88 (0.84−0.92)
Intercept (95% CI)	0.21 (-0.45 – 0.91)
Bias @120 µg/g	-14.1 (-15.7 − -9.2)
R^2	0.967

Qualitative agreement measures derived from the Q.S.E.T. Device Plus were compared to the Q.S.E.T. collection method to evaluate the comparative performance of Q.S.E.T. Device Plus.

Qualitative performance of Q.S.E.T. Device Plus-extracted samples compared to predicate					
		Predicate (Q.S.E.T. Device)			
		(+)	Equivocal	(−)	
Q.S.E.T. Device Plus	(+)	44	0	0	44
	Equivocal	1	14	0	15
	(−)	0	2	98	100
		45	16	98	159
Equivocal considered negative (−)		PPA (95% CI): 97.8% (88.4−99.6%)			
		NPA (95% CI): 100% (96.7−100%)			
Equivocal considered positive (+)		PPA (95% CI): 96.6% (88.5−99.1%)			
		NPA (95% CI): 100% (96.2−100%)			

2. Matrix Comparison:

Not applicable, as stool is the only sample matrix for this assay.

C Clinical Studies:

Clinical performance for the LIAISON Calprotectin assay was evaluated in K182698.

D Clinical Cut-Off:

Clinical performance for the LIAISON Calprotectin assay was evaluated in K182698.

E Expected Values/Reference Range:

Reference intervals and expected values for the LIAISON Calprotectin assay were evaluated in K182698.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.